THE ROLE OF SERINE IN GROWTH AND INTERMEDIARY METABOLISM

BY

HENRY JAMES SALLACH

B. S., University of Nebraska, 1944

M. S., University of Nebraska, 1947

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY
IN CHEMISTRY IN THE GRADUATE COLLEGE
OF THE UNIVERSITY OF ILLINOIS, 1950.

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I. THE ROLE OF SERINE UNDER DIETARY CONDITIONS INVOLVING ITS USE FOR SYNTHETIC PURPOSES

Introduction

The amino acid serine is now known to serve at least five major functions in the animal organism, namely, (a) as a component of proteins, (b) as a constituent of cephalins (1), (c) as a precursor of ethanolamine and hence of choline (2), (d) to furnish the carbon chain necessary for the synthesis of cystine (3), and (e) as one of the precursors of glycine (4).

In view of the above facts it was desired to determine whether the simultanous removal of serine, glycine, and most of the choline from the diet of rats would tax their synthetic functions sufficiently to limit the rate of gain. After these tests had been finished, the project was extended to include a comparison of the growth of animals (a) on a complete diet except for slightly deficient levels of methionine and threonine, and (b) a similar ration from which serine, glycine, cystine and most of the choline had also been excluded.

Experimental

Weanling white rats from the stock colony served as the experimental subjects. The duration of the two tests was twenty--eight and thirty-six days respectively. The synthetic amino acid mixtures used were modifications of Mixture XXIII (cf. 5) which has been extensively employed in this laboratory. All synthetic diets were appropriately supplemented with vitamins.

Summary

The results have shown that the simultaneous removal of serine and glycine from the diet of the rat does not affect detectably the rate of growth.

With the ration which was devoid of serine, glycine, cystine, and most of the choline, a significant inhibition in growth was observed. The **multiple** deficiency resulting from the absence of all of the above components may have, and probably did, contribute to the slower rate of gain. However, since these constituents are so closely related metabolically, and since serine occupies an intermediate position among them, the absence of the latter must have been one of the limiting factors.

These results reemphasize the remarkable ability of the organism in manufacturing the non-essential amino acids. Only under circumstances which impose a terrific synthetic burden does growth inhibition occur.

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II. THE FATE OF GLYCERIC ACID AND ITS RELATIONSHIP TO SERINE SYNTHESIS IN THE ANIMAL BODY

Introduction

Little is known concerning the origin of serine in the intact animal. Evidence has been presented which indicates that serine arises from glycine (1, 2) and that glycine, in turn, is formed from serine (3). Although these two amino acids appear to be interconvertible in the animal organism, there is no indication as to the source of the original carbon chain employed in their synthesis. The present study was undertaken with the hope of determining, if possible, a source of the carbon chain of serine. For this purpose, glyceric acid labeled with C^{14} in the carboxyl group was synthesized and administered to rats. Serine was then isolated from the tissues and tested for radioactivity. At the same time, glycogen was separated from the livers and samples of glycerol were obtained from body fat. Each of these was tested for activity. In the case of one animal, the expired carbon dioxide, urine, and feces were separately collected and analyzed for C^{14}.

Experimental

Glyceric acid was prepared from glycolaldehyde by the addition of hydrogen cyanide containing C^{14} and hydrolysis of the resulting nitrile. Serine of the tissues was precipitated from an aqueous solution of a glacial acetic acid-insoluble fraction of the neutral amino acids as its p-hydroxyazobenzene-p-sulfonate. Glycogen was extracted from the livers with trichloroactic acid. Glycerol was obtained by hydrolysis of a sample of body fat.

Summary

Approximately 72.5 per cent of the isotope present in the glyceric acid was recovered in the expired air during the twenty-four hour interval following the administration of the compound. The urine contained only 0.96 per cent. The feces contained an insignificant amount which probably was derived from contamination by small amounts of urine.

Serine isolated from the carcasses of the animals and from the combined livers showed the presence of significant amounts of C^{14}. The concentration of the liver serine was approximately four times that of the carcass serine. These findings demonstrate that glyceric acid is transformed, in part, into the amino acid.

Glycerol isolated from tissue fats and glycogen separated from the livers contained very high concentrations of C^{14}. These facts confirm the ideas expressed in the literature, as a result of the application of other techniques, that glyceric acid is a glycogen former and can be reduced in the organism with the production of glycerol.

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VITA

The author was born on July 15, 1922, in Albion, Nebraska. He attended the public schools there, and was graduated from Albion High School in May, 1940. In September, 1940, he entered the University of Nebraska, and received a Bachelor of Science degree from that institution in June, 1944. He was employed as an analytical chemist until September, 1946, at which time he entered the Graduate College of the University of Nebraska. He received the Master of Science degree in August, 1947. Since entering the Graduate College of the University of Illinois in September, 1947, he has held a research assistantship for two years, and an Atomic Energy Commission Fellowship for one year.